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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,864	06/28/2001	Keiichi Yokoyama	209524US0 CONT	3226

22850 7590 02/05/2003

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1940 DUKE STREET
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EXAMINER

PATTERSON, CHARLES L JR

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 02/05/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/892,864

Applicant(s)

YOKOYAMA ET AL.

Examiner

Charles L. Patterson, Jr.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 6/28/01, 4/16/02, 5/23/02 and 11/14/02.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-75 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-75 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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After reading applicants arguments concerning the restriction requirement and the specification, the requirement is hereby dropped. The examiner will examine claims 1-75.

It is noted for the record that the PCT corresponding to the instant application has not been received. The examiner retrieved a copy of it but it was in Japanese. Also, a sworn translation of the Japanese patent application priority document has not been received. Therefore the following action is made using only the date of filing the instant application (6/28/01) as a priority date.

The disclosure is objected to because of the following informalities:

On page 30, line 13, "Example 21" is referred to. This is confusing because there are only 16 examples in the instant specification.

Appropriate correction is required.

Claims 1, 9, 23-34, 36, 38 and 44-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 38 are indefinite in the recitation of "acidic aqueous medium" and "neutral pH". It is unclear from the recitations what pH these two solutions are. An "acidic aqueous medium" could be at any pH below 7.0 and a "neutral pH" could be interpreted as being a wide range of values.

Claims 9 and 46 are confusing and indefinite in the recitation of "from 40 mg/ml" on line 2. There are not two numbers indicating the lower and up-

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per limits of the concentration and therefore the instant phrase is indefinite and confusing.

Claims 23 and 24 are confusing and indefinite in the recitation of "the inorganic salt accelerator". There is no antecedent basis for this phrase in claim 21.

Claims 25 and 26 are confusing and indefinite in the recitation of "the organic salt accelerator". There is no antecedent basis for this phrase in claim 21.

Claims 27 and 28 are confusing and indefinite in the recitation of "the amino acid salt accelerator". There is no antecedent basis for this phrase in claim 21.

Claims 29 and 30 are confusing and indefinite in the recitation of "the polyol accelerator". There is no antecedent basis for this phrase in claim 21.

Claims 31 and 32 are confusing and indefinite in the recitation of "the organic solvent accelerator". There is no antecedent basis for this phrase in claim 21.

Claims 33 and 34 are confusing and indefinite in the recitation of "the surfactant". There is no antecedent basis for this phrase in claim 21.

Claim 36 is indefinite and confusing in the recitation of "has an intermediate structure..." What is intended by this phrase? Is it perhaps the transglutaminase that has been treated with pH 4.0 conditions?

Claims 44-46 are indefinite in the recitation of "the protein denaturant", which term does not have antecedent basis.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear,

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concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for producing a transglutaminase using the conditions in Examples 1-16, does not reasonably provide enablement for producing the transglutaminase under the requirements of the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification teaches that transglutaminase was denatured in 8 M urea and 20 mM DTT, then the pH was adjusted to 4.0 in buffer containing the same 8 M urea and 20 mM DTT, cooled to 5° C and then the urea concentration was lowered and the pH adjusted to 6.0. There is nothing in the instant specification teaching that any of these ingredients and steps are not necessary to obtain the re-natured enzyme of the instant claims and without proof to the contrary it is maintained that they are.

Claim 75 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant specification does not teach a transglutaminase that has a "lower mobility than that of a native state in native-polyacrylamide gel electrophoresis with a His-Mes buffer system at pH 6.1". Example 16 teaches that in a native gel "the mobility was unchanged before and after the change in the composition of the solvent". Figure 13 is the only native gel shown in the instant specifi-

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cation and there is no evidence that the enzyme of claim 75 has a "lower mobility than that of the native state". Is claim 75 claiming the enzyme in the "intermediate state", i.e. at pH 4.0?

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-19, 21-56, 58-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshikawa, et al. (AO). The instant reference teaches the solubilization and re-naturation of a biologically active protein by lowering the pH to 4.0 and then ultimately raising the pH to 8.5. The biological activity of the protein was restored after the process as discussed in the paragraph spanning pages 8-9. It would have been obvious to one of ordinary skill in the art to treat denatured transglutaminase according to the same methods used in the instant reference with the expectation that biological activity would be restored, absent unexpected results. Anything not specifically taught in the instant reference would have been obvious, absent a convincing showing to the contrary.

Claims 1-10, 13-19, 21-47, 50-56 and 58-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ejima, et al. (AY). The instant reference teaches that interleukin-6 may be re-natured by first treating at pH 5.5 and then raising the pH to 8.5. It would have been obvious to one of ordinary

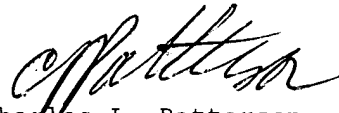
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skill in the art to treat denatured transglutaminase according to the same methods used in the instant reference with the expectation that biological activity would be restored. Anything not specifically taught in the instant reference would have been obvious, absent a convincing showing to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 703-308-1834. The examiner can normally be reached on Monday - Friday, 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone number is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
February 3, 2003